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THERAPEUTIC USE OF EXOSKELETONS IN SPINAL CORD
INJURY GAIT REHABILITATION – A SYSTEMATIC
LITERATURE REVIEW

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The purpose of this thesis was to research the effectiveness of using exoskeletons in robot-assisted therapy for gait restoration in people with spinal cord injury (SCI). The research for this thesis was carried out in a form of a literature review to address the effectiveness of exoskeletons in improving walking speed and walking distance compared to other physiotherapeutic approaches. The theoretical content of the thesis includes background on spinal cord injuries with anatomy of the spinal cord, modalities used in rehabilitation of gait in population with spinal cord injuries and a presentation of different exoskeletons that are used in robot-assisted gait rehabilitation.

The search for full and freely available articles was made using four different databases: Medline/Pubmed, Cochrane Library, Ebsco Host and Science Direct. Four different articles were found but only three of them were assessed further after applying the PEDro scale. All studies used the same type of exoskeleton (Lokomat) and compared it to other approaches.

Robot-assisted gait rehabilitation was found not to be any more effective compared to other modes of physiotherapy, such as treadmill-based training with manual assistance, treadmill-based training with stimulation, overground training with stimulation, and strength training. It appears that conventional gait training on a treadmill and muscle strength training yield better results in walking speed and distance, and overground locomotor training shows greater improvements in functional walking capacity than treadmill-based training.

CONTENTS

| | | |
|-----|---|----|
| 1 | INTRODUCTION | 4 |
| 2 | SPINAL CORD INJURY | 5 |
| 2.1 | Anatomy of the spinal cord..... | 5 |
| 2.2 | Classification of spinal cord injuries..... | 8 |
| 2.3 | Gait ability in spinal cord injuries..... | 9 |
| 2.4 | Gait rehabilitation in spinal cord injuries..... | 12 |
| 3 | ROBOT-ASSISTED GAIT REHABILITATION | 13 |
| 3.1 | Exoskeletons | 14 |
| 3.2 | Lower limb exoskeletons | 14 |
| 3.3 | Exoskeletons available for gait rehabilitation..... | 20 |
| 3.4 | Limitations of lower limb exoskeletons..... | 24 |
| 3.5 | Previous research on exoskeletons..... | 24 |
| 4 | PURPOSE OF THE THESIS | 26 |
| 5 | RESEARCH METHOD AND PROCESS | 26 |
| 5.1 | Thesis process | 26 |
| 5.2 | Systematic literature review | 27 |
| 5.3 | Search strategy | 27 |
| 5.4 | Study selection | 28 |
| 5.5 | Methodological quality assessment | 30 |
| 6 | RESULTS..... | 33 |
| 7 | CONCLUSION | 34 |
| 8 | DISCUSSION | 35 |
| | REFERENCES..... | 37 |

1 INTRODUCTION

Spinal cord injury (SCI) is a debilitating condition that affects many aspects of a person's life, including the ability to walk. For those with incomplete spinal cord injury or low complete spinal cord injury who have a potential to walk again there are different modes of physiotherapy that are used in gait rehabilitation (Harvey 2008). One of them is robot-assisted rehabilitation that uses different exoskeletons for restoration of motor function. Gait training is a form of motor learning, and therefore has to be intense, repetitive, well structured, task- and context-specific in order to enhance motor recovery and potentially restore motor function (Koceska & Koceski 2013).

Robotics for healthcare is an emerging field and it is expected to grow in the future. It can replace the physical effort of a therapist, allowing for more intensive repetitive motions and delivery of therapy at a reasonable cost, as well as accurately measure the force and movement patterns during motor recovery (Diaz et al. 2011).

Nowadays several different exoskeleton systems are used in rehabilitation centres and many are being developed and undergoing testing. They focus on providing missing movements and sensing, safer environments, and environments that make regaining movement-related function easier and faster. They aim to provide dexterity, natural mobility and even sense of touch to missing or paralyzed limbs (Dellon & Matsuoka 2007, 30).

2 SPINAL CORD INJURY

Spinal cord injury (SCI) is damage to the spinal cord that results in partial or complete motor or sensory loss. Most often it is a consequence of a trauma, such as a motor vehicle accident or fall, sport injuries or work-related injuries, but it can also result from illness, infection or congenital defect. A typical person with a spinal cord injury is a male aged between 15 and 25 years (Harvey 2008, 3). Every year, around the world, between 250,000 and 500,000 people suffer a spinal cord injury. Males are most at risk in young adulthood (20-29 years) and older age (70+). Females are most at risk in adolescence (15-19) and older age (60+). Studies report male-to-female ratios of at least 2:1 among adults, sometimes much higher (Website of World health organisation, 2017). About 5% of spinal cord injuries occur in children as a result of a road trauma or fall from height, and they sustain a complete spinal cord injury more often than adults (Grundy & Swain 2002, 1). In Finland, the estimated number of people with a traumatic spinal cord injury is 3000 (Website of Käypä hoito, 2014).

Injury can happen at any level of the spinal cord. Over 55% of injuries affect the cervical spine which results in *tetraplegia* (also called quadriplegia) where trunk and all four limbs are affected. The rest of the injuries affect thoracic, lumbar or sacral spine in similar proportions and result in *paraplegia* where only the lower limbs and trunk to some degree are affected. The most common level of spinal cord injury is C5, followed by C4, C6 and T12 (Harvey 2008, 3).

2.1 Anatomy of the spinal cord

Spinal cord is a long, thin bundle of nerves that passes from the base of the brain (brainstem) to the lumbar region of the vertebral column. It typically terminates between levels T12 and L2. Together with the brain it forms the central nervous system (CNS). The spinal cord is protected by the surrounding vertebrae, vertebral ligaments, connective tissue coverings, and cerebrospinal fluid (Tortora & Derrickson 2011, 492-493).

The spinal cord appears to be segmented the same way as the spine because the 31 pairs of the spinal nerves emerge from intervertebral foramina. The number of nerve pairs that exit the spinal cord corresponds to the number of vertebrae in the spine segments, except for the cervical segments. There are 8 pairs of cervical nerves (C1-C8), 12 pairs of thoracic nerves (T1-T12), 5 pairs of lumbar nerves (L1-L5), 5 pairs of sacral nerves (S1-S5) and 1 pair of coccygeal nerves (Co1) (Tortora & Derrickson 2011, 494-498).

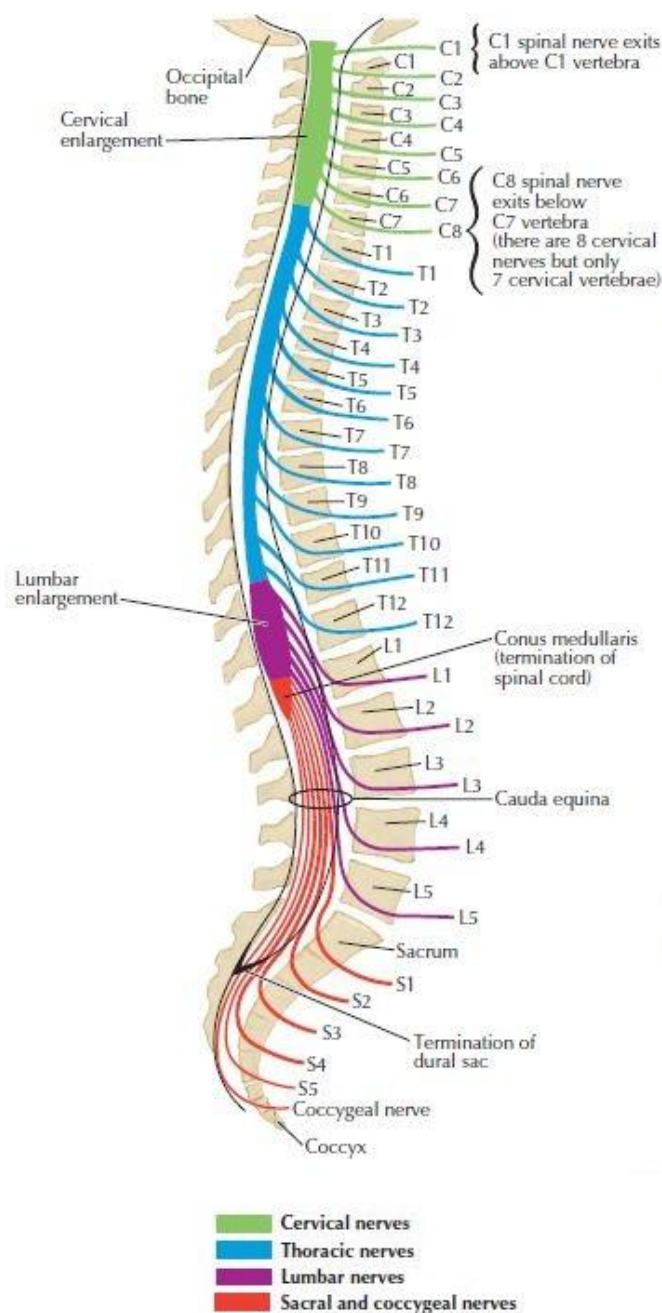


Figure 1. Anatomy of the spinal cord (Netter 2014, 161).

Each corresponding nerve root exits the spine in a specific pattern and this pattern differs between the cervical and the thoracic/lumbar regions. The spinal nerves exit the cervical spine *above* their corresponding vertebral body level. For example, the C7 nerve root exits above C7 through the C6-C7 neural foramen. C8 exits in between T1 and C7, since there is no C8 vertebral body level. This orientation is reversed in the thoracic and lumbar spine. The thoracic and lumbar spinal nerve roots exit *below* their corresponding vertebral body level. For example the L3 nerve root exits below L3 through the L3-L4 foramen (Tortora & Derrickson 2011, 500).

Each spinal nerve is connected to a segment of the cord by a posterior and an anterior root and their rootlets. The posterior (dorsal) root and rootlets contain only sensory axons which conduct nerve impulses from sensory receptors in the skin, muscles and internal organs into the CNS. The anterior (ventral) root and rootlets contain axons of motor neurons, which conduct nerve impulses from the CNS to muscles and glands (Tortora & Derrickson 2011, 494-498).

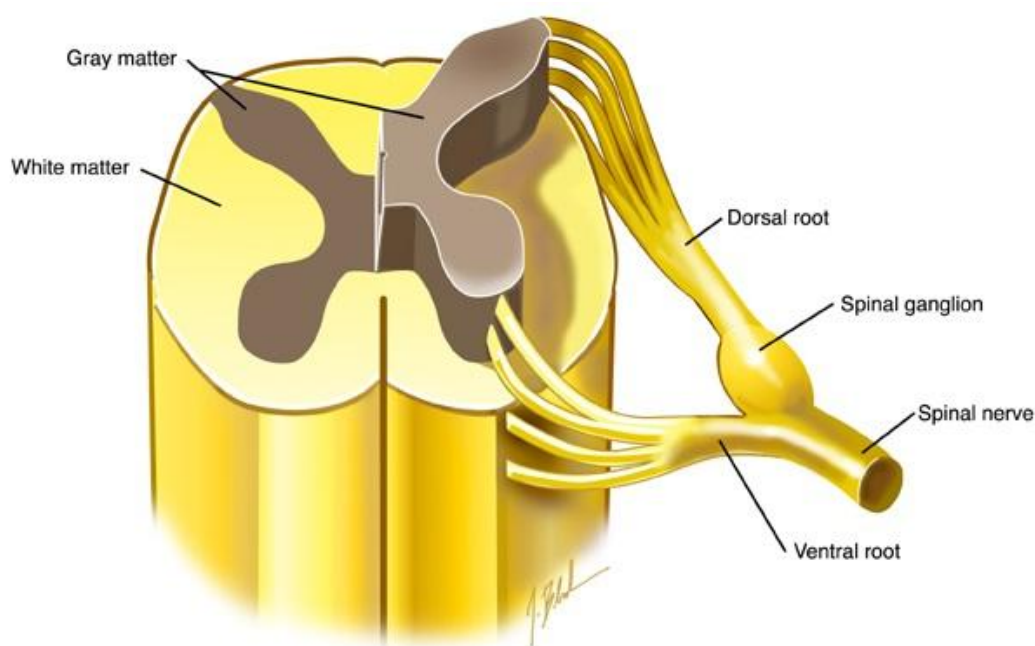


Figure 2. Structure of the spinal cord (Website of Back pain guide, 2017).

The spinal cord conveys electrical impulses between different parts of the body and the brain, and together with its associated spinal nerves controls some of our most rapid reactions (reflexes) to environmental change. Any damage to the spinal cord may, therefore, cause permanent changes in strength, sensation and other body func-

tions (e.g. bladder and bowel control, sexual function) below the site of the injury (Bromley 2006, 13).

Spinal cord has an ability to repair itself to a certain degree, even after a spinal cord injury. That is due to the neural plasticity, the capacity of neurons and their axons to regenerate in order to restore neuronal function and recovery. This means that motor, sensory and autonomic functions can spontaneously recover to various extents regardless of the level of the injury or whether the injury was complete or incomplete (Onifer et al. 2011). However, the degree of functional recovery depends on the amount of spared neurons, location of the lesion, and activity during the rehabilitation. It has been shown that rehabilitative training, especially treadmill locomotor training has large effects on cellular and molecular function involved in plasticity and can promote plasticity to a great extent (Fouad et al. 2011).

2.2 Classification of spinal cord injuries

Neurological damage of the spinal cord can involve transection of the spinal cord or it can be secondary to vascular and pathogenic events such as inflammation, oedema and changes to the blood-spinal cord barrier. In the latter case the spinal cord remains intact. Depending on the extent of the damage to the cord, all or just some neural messages will be transmitted across the site of the lesion. Thus the injury can be complete or incomplete (partial). In incomplete injuries there is a highly variable preservation of motor and sensory pathways below the level of injury, therefore some persons may have only slight movement or sensation whereas others can walk almost normally. Incomplete injury is more common following cervical, lumbar or sacral injuries than thoracic injuries, and it is more common nowadays due to improvement of emergency on-site management and acute management (Harvey 2008, 4).

Severity of spinal cord injury is classified based on ASIA (American Spinal Injury Association) Impairment Scale (AIS). This is a five point ordinal clinician-administered scale that identifies the sensory and motor levels indicative of the highest spinal level demonstrating “unimpaired” function. Preservation of function in the sacral segments (S4-S5) is a key for determining the AIS grade. Manual muscle test-

ing of ten key muscle groups for motor levels, and pin prick and light touch testing for sensory levels are administered to help determine the AIS grade (Stokes & Stack 2012, 57-58). AIS grades are presented in the Table 1 (Kirshblum et al. 2011, 543).

Table 1. AIS grade system.

| | | |
|----------|--------------------|---|
| A | Complete | No motor or sensory function is preserved in the sacral segments S4-S5. |
| B | Sensory incomplete | Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5 AND no motor function is preserved more than three levels below the motor level on either side of the body. |
| C | Motor incomplete | Motor incomplete. Motor function is preserved below the neurological level and more than half of key muscle functions below the single neurological level of injury have a muscle grade less than 3. |
| D | Motor incomplete | Motor function is preserved below the neurological level and at least half of key muscle functions below the neurological level of injury have a muscle grade of 3 or greater. |
| E | Normal | If sensation and motor function are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade |

2.3 Gait ability in spinal cord injuries

The main consequences of an SCI are, among others, inability to walk, impaired walking, and disability resulting from paralysis of the muscles in the lower limbs. Many people with a SCI will wonder whether they will be able to walk again. In therapy setting, a mutual understanding of what is walking is needed both for the client and the therapist: whether walking means merely moving from point A to point B

or does walking imply symmetrical and coordinated movements that resemble those before the patient's injury; is the goal household ambulation or to some degree community ambulation; does walking allow physical assistance and use of assistive aids or is it independent (Behrman, Druin, Bowden & Harkema 2009).

According to Whittle (2007, 48), "normal" walking (ambulation) is a method of locomotion that involves the use of the two legs, alternately, to provide both support and propulsion, where at least one foot is in contact with the ground at all times. Gait is the manner or style of walking rather than the walking process itself, but it will be used in this thesis synonymously with the term walking. Whittle then continues that in order for a person to walk, the locomotor system must be able to accomplish four things without apparent difficulty and with modest energy consumption. These are: each leg has to support the body weight without collapsing, balance (static or dynamic) must be maintained during single leg stance, the swinging leg must be able to move to a position where it can take over the supporting role, and lastly, sufficient power is needed for necessary limb and upper body movements. In pathological gait these requirements can be met by compensating with abnormal movements, which are usually more energy consumptive, or by the use of walking aids such as canes, crutches or orthoses. If even one of these four requirements cannot be met, the subject is unable to walk (Whittle 2007, 101).

A good prognostic indicator for ambulation is a preserved sacral sensation for pain and temperature which indicates sparing in the spinothalamic tracts. Without spinothalamic tract sparing, the likelihood of ambulation decreases to approximately 10% - 33% (Behrman et al. 2009, 381). Approximately 50% of people with spinal cord injury walk. Children generally attain a higher level of upright mobility than adults which might be due to biomechanical advantages of being a child or extensive support provided by schools, parents and therapists. However, neurological status is the strongest predictor of capability to walk. People with tetraplegia and total paralysis of lower extremities (ASIA A or B) cannot walk. They can stand with frames, tilt tables or standing wheelchairs for the therapeutic benefit of being upright and weight-bearing through lower extremities (Harvey 2008, 107).

People with thoracic paraplegia and total paralysis of lower extremities (ASIA A or B) usually stand for exercise, although they can ambulate with walking aids on level ground if they have good upper limb strength and extensive orthotic support. Bilateral knee–ankle–foot orthoses (KAFO) and different types of hip–knee–ankle–foot orthoses (HKAFO) are used together with elbow crutches or frame. They enable either a reciprocal or jumping gait pattern. However, their gait is slow and energy-consuming. Walking aids also limit use of hands during walking for tasks such as cooking and carrying bags (Harvey 2008, 107-118).

Most people with motor incomplete lesions (ASIA C, D or E) and lumbosacral paraplegia can walk for at least limited distances. People with ASIA lower extremity motor scores *less than* 20/50 generally use wheelchairs as their primary form of mobility. They may walk around the home or for the purposes of therapeutic exercise, using orthoses and aids. People with ASIA lower extremity motor scores *more than* 20/50 generally attain the capacity for community ambulation and are capable of walking at reasonable speeds. People with incomplete tetraplegia who are dependent on walking aids generally require more strength in their lower extremities than those with paraplegia in order to adequately compensate for their upper limb weakness. The situation with incomplete lesions is more complex because some muscles are paralysed and others are not. Thus people with incomplete lower limb paralysis develop compensatory movements during gait, e.g. “hip hiking” or circumduction of the entire leg in paralysed dorsiflexor muscles; hyperextension of knees in paralysed quadriceps muscles etc. They, too, require orthoses and splints (Harvey 2008, 107-128).

People tend to choose the most practical, fast, efficient and functional way of moving about in the community. Where the environment is accessible for wheelchairs, a wheelchair is an efficient form of transport. However, in areas with mountainous terrain without wheelchair accessibility walking may be the only option for mobility. There are many benefits to regaining ambulatory function after SCI. Weight bearing helps prevent osteopenia that often accompanies acute SCI, standing and walking may decrease spasticity, incidence of pressure ulcer formation, urinary tract infections, and it may have positive impact on bladder and bowel regulation. Walking also has psychological impact on the individual with SCI and improves quality of life,

such as sleep, fatigue management and general well-being (Behrman et al. 2009, 381).

2.4 Gait rehabilitation in spinal cord injuries

According to Koceska & Koceski (2013, 1), the goal of gait therapy is to “re-train the nervous system, to re-build muscle strength, to improve balance and to re-train kinematics in order to reduce the stresses applied to bones and muscles”. Furthermore, gait training is a form of motor learning, and it has to be intense, repetitive, well structured, task- and context-specific in order to enhance motor recovery and potentially restore motor function. Repetitive practice strengthens neural connections involved in a motor task through reinforcement learning (Koceska & Koceski 2013, 1-2). Gait training needs to involve stepping and walking in an upright and weight bearing position (Harvey 2008, 149).

There are three different modalities of gait rehabilitation: conventional gait training, partial bodyweight support (PBWS) treadmill gait rehabilitation with manual assistance, and robot-assisted gait rehabilitation. Several factors should be considered before commencing conventional gait training in people with SCI, such as individual’s motor control, range of motion (ROM), muscle tone, sensation, functional abilities, posture, skin integrity, and autonomic function (Behrman et al. 2009, 382).

Conventional gait training includes strengthening and endurance training of muscles under voluntary control. Training is specific, tailored to the individual and usually involves practising of one single movement at time. To compensate for deficits of paralysed or weakened muscles, therapists use different orthoses, braces and assistive devices for support. Training typically begins in parallel bars. The parallel bars allow the patients to support themselves with their upper body strength, and gradually put more weight on their legs as they regain the ability to walk. For safety reasons, a harness can be used. Later, rehabilitation progresses to walking with assistive devices, e.g. walking frame, rollator, crutches (Koceska & Koceski 2013, Behrman et al. 2009, 384).

Partial bodyweight support (PBWS) treadmill gait rehabilitation uses a suspension system (harness) to provide proper upright posture, balance and safety. Usually two or three physiotherapists manually assist the moving of the patient's legs during training and therefore coordinate the walking. The BWS reduces the demands on muscles which may enable the patient to focus more on improving coordination of movements while gradually increasing muscle strength. As the patient progresses, the bodyweight support can be gradually decreased, which challenges the patient to maintain more balance and postural control (Koceska & Koceski 2013, 2).

Robot-assisted gait rehabilitation is a fairly new mode of gait rehabilitation that uses different types of robots to assist in gait training. It is a general assumption that with further technological development robotics will play an important role in therapeutic activities within rehabilitation treatment. More on robot-assisted gait rehabilitation is presented in the next chapter.

3 ROBOT-ASSISTED GAIT REHABILITATION

Traditional gait rehabilitation therapies often require several therapists together to manually assist the legs and torso during gait training. This type of training is labour-intensive and exhaustive, so it cannot be carried out for a long period of time. Therefore it may limit the full potential of the treatment. It also presents a high economic burden to a healthcare system. Robotic rehabilitation can provide consistent and efficient therapy by replacing the physical effort of a therapist, allowing more intensive repetitive motions with fewer therapists on-site and thus lowering the costs of a therapy. Furthermore, robotic rehabilitation can accurately measure and track patient's motor recovery over the rehabilitation course (Diaz et al. 2011).

The key principle behind robotic therapy is that repetitive proprioceptive input from the limbs stimulates neuroplasticity in the brain and spinal cord, which in turn restores the mobility of the limbs. There is a greater activation over the sensorimotor cortical regions S1 and S2 as well as cerebellar region after body weight supported

treadmill training (BWSTT) in people with SCI. This implies that BWSTT may augment supraspinal plasticity in brain regions that are related to locomotion (Winchester et al. 2005).

3.1 Exoskeletons

Robotic devices used in robot-assisted rehabilitation are also termed “wearable robots” or “exoskeletons” because they are in certain way attached to the human body. More precisely, an exoskeleton is a mechanical structure with joints and links corresponding to those in the human body. Generally, an exoskeleton can be attached to upper limbs, lower limbs or to the whole body (Sale et al. 2012). Mobile or portable exoskeletons require batteries and a control system usually in a user-worn backpack (Lajeunesse et al. 2015).

Although exoskeletons have been used in gait rehabilitation only for the last two decades, the concept of an exoskeleton as a “mobility assistant” was introduced already in 1883 by prof. H. Wangenstein (Pons 2008: 5). Almost a century after, in 1968, the researchers of University of Wisconsin started to develop a full lower limb exoskeleton, designed to assist paraplegics with complete upper limb capabilities to walk again. With that exoskeleton it was possible to walk at 50% of normal speed, and implement sit-to-stand and stand-to-sit transfers. In 2000, a treadmill-based exoskeleton Lokomat was developed in Switzerland. Lokomat has been used widely in rehabilitation settings over the past years. Numerous other exoskeletons were being developed in the 21st century (Guan et al. 2016). It has to be noted that exoskeletons have been used in other domains than rehabilitation, for instance in defence and homeland security, military, industry, space, and they have played a role as service robots for instance in rebuilding nuclear power plants, caring for the elderly, keeping watch at museums and similar (Pons 2008: 11).

3.2 Lower limb exoskeletons

Several lower-limb exoskeletons have been developed to restore mobility of the affected limbs in gait rehabilitation. They can be powered exoskeletons which require

batteries or electricity, passive exoskeletons which do not require electrical power source, and hybrid exoskeletons which are powered but use functional electrical stimulation (FES) of the muscles and actuators. They can be also either fixed, meaning that the device is attached to a wall, a bracket or suspended from the air by a fixed hook and harness, or mobile, where the user and the exoskeleton move around freely (Website of Exoskeleton report 2017).

Fixed exoskeletons are either treadmill based or foot-plate based. An example of a treadmill based exoskeleton is Lokomat (manufactured by Hocoma AG) which consists of a robotic gait orthosis and an advanced bodyweight support system, combined with a treadmill. Computer controlled motors are integrated into bilateral hip and knee joint of the orthosis. Lokomat is most clinically evaluated system (Diaz et al. 2011, 2). Other treadmill-based exoskeletons are G-EO System, KineAssist, ReoAmbulator, RoboGait, and Walkbot.



Picture 1. Lokomat (picture is courtesy of Hocoma, Switzerland).

Foot-plate based exoskeleton has programmable separate foot plates in which the feet of the patient are positioned and moved by robotic system to simulate different gait patterns. The patient is secured by a harness. Only one such system is in the market, named Gangtrainer GT 1, which is at least as effective as the manual treadmill therapy but it requires less input from the therapist (Diaz et al. 2011, 4).



Picture 2. Gangtrainer GT 1 (picture is courtesy of Reha Stim, Germany).

Mobile or portable exoskeletons are those where the user and the exoskeleton move over ground freely. They are attached to the patient with motorized hip and knee joints and the patient wears a backpack with a battery and controller. Most such exoskeletons require the use of crutches for balance while walking. Main difference between mobile and treadmill based exoskeletons is that mobile exoskeletons allow patients to apply natural gait training (Chen et al. 2013). Examples of mobile exoskeletons are ReWalk, Ekso GT, Indego, HAL, and REX.

Assistance needed in exoskeletal stepping varies from minimal to moderate, but is it also possible to control the exoskeleton without any assistance. A powered exoskeleton uses different mechanisms to control walking: it can be either »user-operated via buttons« by pressing the buttons of the walker or it can be »user-operated via own shifts«, where the user shifts own weight within the exoskeleton, the exoskeleton detects changes in the centre of mass over one limb and in response generates a step contralaterally. Another mechanism is to initiate stepping by an »external operator« using a control interface (Louie et al. 2015, 5).

ReWalk exoskeleton is designed primary for clinical use but ReWalk personal 6.0 model can be also used as a training tool for home use. The exoskeleton's system

senses patient's forward tilt of the upper body and thus initiates the first step. Repeated body shifting generates a sequence of steps which mimics a functional natural gait of the legs (Website of ReWalk Robotics 2017).



Picture 3. ReWalk (picture is courtesy of ReWalk Robotics).

Indego is a hip-knee powered exoskeleton which implements hybrid functional electrical stimulation (FES) system to stimulate muscle activity. There are two models; Indego Therapy is used in rehabilitation and Indego Personal at home and in the community (Website of Exoskeleton Report 2017, Chen et al. 2013, 351).



Picture 4. Indego Therapy exoskeleton (picture is courtesy of Indego).

Ekso GT (previously named eLEGS, Exoskeleton Lower Extremity Gait System) was developed in 2010 and it is the first exoskeleton approved by FDA for patients recovering from stroke as well as for those with SCI levels of T4-L5 and levels of T3-C7. In 2016 there were a little fewer than 200 Ekso GT units used worldwide (Website of Eksobionics 2017).



Picture 5. Ekso GT, applying sit-to-stand function (picture is courtesy of EksoBionics).

HAL Lower Limb is the most widely distributed mobile medical rehabilitation exoskeleton. It is a powered hip-knee wearable robot with a bio-electrical signal control scheme. Its control system processes data from surface electromyography (EMG) sensors, angle/acceleration sensors, and force sensors to estimate the necessary forces to assist the user's intended actions. The use of EMG signals in HAL's shared control system to help detect the user's intent represents a type of hybrid peripheral neural interface (He et al. 2017, 93).



Picture 6. HAL Lower limb exoskeleton for medical use (picture is courtesy of Cyberdyne Inc.).

REX is the world's first hands-free, self-supporting, independently controlled exoskeleton which does not require crutches or a walking frame, thus leaving the arms free for upper-body exercises and activities of daily living. It can lift patients from a sitting position into a robot-supported standing position, walk, turn and it can be used in the stairs (Lajeunesse et al. 2015). Another self-balancing exoskeleton, ATALANTE, is designed to provide the full power needed for walking. It launched first clinical trials for validation of the exoskeleton's ability to stand up, walk and sit down with its user safety during 2017 and is currently still being evaluated for gait rehabilitation (Website of Wandercraft 2017).



Picture 7. REX (picture is courtesy of Rex Bionics).

In therapy setting, apart from training locomotion with an exoskeleton, other aspects can be trained while the patient is wearing the exoskeleton. Depending on whether the exoskeleton provides stability without using the forearm crutches or not, upper body training can be performed. Rex is one of such exoskeletons that does not require use of crutches, which enables the patient to use upper limbs freely. The company of Rex Bionics has developed an exercise program called “rexercises” to address strength, flexibility, balance and endurance with minimal assistance from the therapist (Website of RexBionics, 2017). See Picture 8.



Picture 8. Rexercises when wearing Rex Exoskeleton (photos are courtesy of Rex-Bionics).

3.3 Exoskeletons available for gait rehabilitation

Treadmill-based exoskeletons weigh between 500 kg (KineAssist) and 1000 kg (Lokomat) and can provide maximum speed of 3.2 km/h when using the gait orthosis (Lokomat) (Website of HDT Global 2017, Website of Hocoma 2017). Mobile exoskeletons have to be lighter because they're worn by a user. They typically weigh between 12 kg (e.g. Indego, PhoeniX) and 20 kg (Ekso GT) and achieve maximum speeds of 1.8 km/h (PhoeniX), 2.5 km/h (e.g. ReWalk) or 3.2 km/h (Ekso GT) with exception of H-MEX exoskeleton which can achieve max speed of 12 km/h. Speed depends on the user's injury level and skills to control the exoskeleton. The price for mobile exoskeletons varies between the cheapest 21,000 € (Axosuit) and 105,000 €

(REX), with average between 60,000 € and 70,000 € (Website of Exoskeleton report 2017).

Table 2 presents powered lower limb exoskeletons that can be used in gait rehabilitation of adult persons with spinal cord injuries. Most mobile exoskeletons are suitable for lower SCI or paraplegia because they require adequate upper body strength to use crutches, with exception of REX and Atalante which are self-balancing and thus can be used also with people with complete cervical SCI. Clinical Specialist; Sherri Wallis from Rex Bionics claims that:

”We aren’t restricted in who can use the device based upon level of spinal injury like the other devices are. Based upon our experience with patients who’ve been successful in REX, we have had individuals with SCI levels of injury as high as C-3 with ventilator dependence in REX with the therapist controlling the joystick. We have also had individuals with locked-in syndrome successfully use REX where they have no movement other than their head” (REX Customer service 2017).

Table 2. Lower limb exoskeletons for gait rehabilitation adult patients with spinal cord injury.

| Exoskeleton's name (producer) | Type of exoskeleton | Target SCI population | Use | Particularities | Availability and price |
|---|----------------------------|-----------------------------------|-------------------------------------|---|--|
| ARKE (Bionik Laboratories, Canada) | Mobile | Lower SCI | Pre-clinical trial phase | Requires crutches | Used in multiple clinics for research in the U.S. Price: 67,200 € |
| ATALANTE (Wandercraft, France) | Mobile | Complete SCI | Rehabilitation and assistive device | Self-balancing | Pre-clinical trial phase Price unknown, |
| Axosuit (Axosuits, Romania) | Mobile | Lower SCI | Rehabilitation (clinical use) | Requires crutches | Still under development Price: estimated to 21,000 € |
| Ekso GT (Ekso Bionics, USA) | Mobile | Complete and incomplete SCI C7-L5 | Rehabilitation (clinical use) | Requires crutches, FDA approved | Price: 59,000 € |
| ExoAtlet (ExoAtlet, Russia) | Mobile | Lower SCI | Rehabilitation, assistive device | Requires crutches | Over 20 ExoAtlets in circulation for medical and personal use in 2016. Price: 58,800 € |
| G-EO system (Reha Technology AG, Switzerland) | Fixed, foot plates, BWS | unknown | Rehabilitation (clinical use) | Stair climbing up and down simulation | |
| H-MEX (Hyundai, South Korea) | Mobile | Lower SCI | Rehabilitation (clinical use) | Requires crutches, Speed 12km/h | |
| HAL (Cyberdyne, Japan) | Mobile | Lower SCI | Rehabilitation (clinical use) | Requires crutches, bio-electrical signal control. FDA approved. | 300 HAL exoskeletons in use in 2016. In 2016 the HAL is not sold but can be rented in Japan and Germany. Price 80,600 |

| | | | | | |
|--|--|----------------|---|--|---|
| | | | | | €. |
| HANK (GOGOA, Spain) | Mobile | Lower SCI | Rehabilitation, assistive device | Requires crutches | In 2016 around 20 HANK exoskeletons in use. Price 67,200 €. |
| Indego (Parker Hannifin, USA) | Mobile | T4 and below | Rehabilitation, assistive device | Requires crutches, Hybrid (FES), FDA approved | Price 58,800 € |
| KineAssist (HDT Global, USA) | Fixed, treadmill-based, safety harness | Incomplete SCI | Rehabilitation (clinical use) | | |
| Lokomat (Hocoma, Switzerland) | Fixed, treadmill-based, BWS | unknown | Rehabilitation (clinical use) | | 782 devices in 359 facilities worldwide. |
| NX-A3 (Guangzhou YiKing, China) | Fixed, treadmill-based, BWS | unknown | Rehabilitation (clinical use) | | |
| PhoeniX (SuitX, USA) | Mobile | Lower SCI | Rehabilitation (clinical use) | Requires crutches, Cannot provide full assistance while climbing stairs. | Price 37,800 € |
| ReoAmbulator (Motorika, USA) | Fixed, treadmill-based, BWS | unknown | Rehabilitation (clinical use) | | |
| ReWalk (ReWalk, USA) | Mobile | Lower SCI | Rehabilitation (clinical use), personal use model | Requires crutches, FDA approved | 200 units in use around the world in 2016. Price 54,600 €. |
| REX (REX Bionics, New Zealand) | Mobile | C3 and below | Rehabilitation (clinical use), personal use model | Self-balancing, Can be used in the stairs | Price 105,000 €. |
| RoboGait (Bama Technology, Turkey) | Fixed, treadmill-based, BWS | unknown | Rehabilitation (clinical use) | | |
| Roki (Roki Robotics, Mexico) | Mobile | T4 and below | Rehabilitation (clinical use) | Requires crutches | It can only be rented within Mexico. Price |

| | | | | | |
|--|---------------------------------------|---------|----------------------------------|--|----------|
| | | | | | unknown. |
| Walkbot (P&S Mechan- ics, South Ko- rea) | Fixed, treadmill- based, BWS | unknown | Rehabilitation (clinical use) | | |

According to Marjo Jännes-Malm (2017) from Fysioline in Finland, Lokomat is used in Hatanpään puistosairaala (Tampere), Laitilan Terveyskoti (Saarenvire), Tornion Sairaskotisäätiö, Kuntoutuskeskus Kitinkannus (Kannus), and there is one Lokomat for paediatric patients at Roboterapia in Vihti. At the moment there is one Indego exoskeleton in use in Finland at Folkhälsan in Mustasaari and Indego exoskeletons can be purchased from their website, fysioline.fi. Price range for purchase of Lokomat in Finland is between 190,000 € and 400,000 € and for Indego between 150,000 € and 280,000 €.

3.4 Limitations of lower limb exoskeletons

Most powered lower limb exoskeletons require use of a gait aid for support during stepping. It is generally expected that exoskeleton users will eventually progress to forearm crutches, which provide less stability than walking frames but are less bulky and thus more portable (Louie et al. 2015, 5).

Physical aspects, such as size, weight, wearing the backpack, and control or movement models of exoskeletons could affect comfort when used in the community. Also battery life and time taken to don and doff the exoskeleton can influence user's satisfaction (Lajeunesse et al. 2016). They may cause some adverse effects, such as skin irritation, pain or discomfort in the shoulder girdle, trunk and muscles of the upper limbs (Platz et al. 2016).

3.5 Previous research on exoskeletons

The use of exoskeletons in rehabilitation has been studied in relation to people with neurological impairments, mostly stroke and SCI. In stroke rehabilitation, there are several studies on upper limb exoskeletons in order to improve arm strength and coordination (Chan et al. 2016, Jarrasse et al. 2014) as well as restoration of hemiplegic

gait in stroke patients. Preliminary findings suggest that gait training with exoskeletons is equivalent to traditional therapy for chronic stroke patients and it can provide additional benefits when combined with conventional methods in sub-acute stroke patients (Louie & Eng 2016).

According to a literature review by Swinnen et al. (2010) there was no evidence that robot-assisted gait training improves walking function in persons with SCI more than other locomotor training strategies. Another systematic review with meta-analysis by Miller, Zimmermann & Herbert (2016) researched effectiveness and safety of powered mobile exoskeletons and concluded that “patients with SCI can safely ambulate in real-world settings at physical activity intensity conducive to prolonged use”. Following an exoskeleton training program, 67% of all patients in that review were able to ambulate with exoskeletons without additional physical assistance. However, most patients included in this review had a complete SCI and thus their rehabilitation would not result in independent walking. Additionally, the studies included in the review did not compare exoskeleton rehabilitation to other physiotherapeutic modalities.

Lower limb exoskeletons have two primary applications: they are used either as an assistive device to enable non-ambulatory individuals with SCI to walk, or as a rehabilitation tool to improve walking ability in ambulatory individuals with SCI (Louie et al. 2015, 1). However, up until today there is no available data to evaluate the effectiveness of exoskeletons used as assistive device in comparison to currently used orthotics (Fisahn et al. 2016). A major advantage of exoskeletons over passive orthoses is that they are powered and can provide coordinated and controlled joint movements rather than rigid knee and ankle fixation (Platz et al. 2016).

4 PURPOSE OF THE THESIS

The purpose of this thesis is to make a literature review on the use of different exoskeletons in rehabilitation of gait in persons with spinal cord injury. The objective is: how effective are exoskeletons shown to be, based on the literature review, compared to other modes of gait rehabilitation. The thesis will also provide a list of exoskeletons for the purpose of gait rehabilitation that are currently on the market and those that are being developed.

The thesis may aid the Well-being Enhancing Technology (WET) research group in SAMK in purchase of an exoskeleton that will, among others, benefit the learning experience of physiotherapy students and others at SAMK.

5 RESEARCH METHOD AND PROCESS

This chapter presents the overall thesis process, research method that was chosen for this thesis (systematic literature review) and the steps that are to be followed when conducting a systematic literature review. That includes an appropriate search strategy, the selection of relevant studies, their quality assessment and summary.

5.1 Thesis process

The topic of this thesis was decided in January 2017 after contacting the Well-being Enhancing Technology (WET) research group in SAMK and agreeing on the topic. Research and collecting of literature started in February, following presentation of the topic at a thesis seminar. Theoretical part was being written from spring 2017 until autumn 2017, and literature review done in autumn 2017. Several exoskeleton companies were contacted by email for additional information on their exoskeletons in November 2017. Gathering of information included also attendance of a webinar organised by one of the exoskeleton companies. Final corrections of the thesis happened in winter 2017.

5.2 Systematic literature review

A systematic literature review is a review that involves a detailed and comprehensive plan and search strategy with the goal of reducing bias by identifying, appraising, and synthesizing all relevant studies on a particular topic (Uman 2011, 57). Khan et al. (2003, 118-121) propose to follow five steps when conducting a systematic literature review: (1) formulation of questions for the review, (2) identification of relevant work, (3) quality assessment of relevant studies, (4) summarizing the evidence, and (5) interpretation of findings.

The first step is to formulate research questions. This is commonly done by identifying the key words connected to the topic, and linking the terms in different ways to form a search strategy, following the Population Intervention Comparison Outcome (PICO) model. In this model the search strategy can be organized based on the topics: population (P), intervention (I), control group (C) and outcome (O). Different combinations of the topics can be made by connecting the terms using AND, OR and NOT to achieve a specific database search outcome (Sayers 2008, 136).

After the search strategy has been completed, the next step is to identify relevant publications to be included in the literature review. This is done by applying inclusion or exclusion criteria while scanning the titles or abstracts of the studies, or even reading the whole papers through. Next step is a methodological quality assessment of the relevant studies. One of the assessment tools is the PEDro (Physiotherapy Evidence Database) quality tool. The final step is to summarize the evidence collected, compare and interpret the results (Khan et al. 2003, 118-121).

5.3 Search strategy

The PICO model was followed in creating search terms, using the conjunctions "AND" or "OR" between the terms:

P = spinal cord injury

I = exoskeleton / robot

C = conventional therapies

O= walking / ambulation / gait / locomotion

The database search was conducted on 21.9.2017. The databases searched were Medline/Pubmed, Cochrane Library, Ebsco Host and Science Direct. The search was undertaken using the following entry terms: “spinal cord injury” AND (exoskeleton OR robot) AND (walking OR ambulation OR gait OR locomotion) in all four databases equally. The search yielded 817 results in total. After applying “humans” and “free full text” or “open access” filters, there were 162 search results (see Table 3).

Table 3. Database search.

| | Medline | Cochrane Library | Science Direct | Ebsco Host | Total |
|--|---------|------------------|----------------|------------|-------|
| Entry terms used | 166 | 13 | 422 | 216 | 817 |
| Humans and open access filters applied | 50 | 13 | 26 | 73 | 162 |

5.4 Study selection

Figure 3 displays the study selection process and the reasons why certain studies were excluded at different stages. There were a total of 817 papers after applying the key-word search in all four databases.

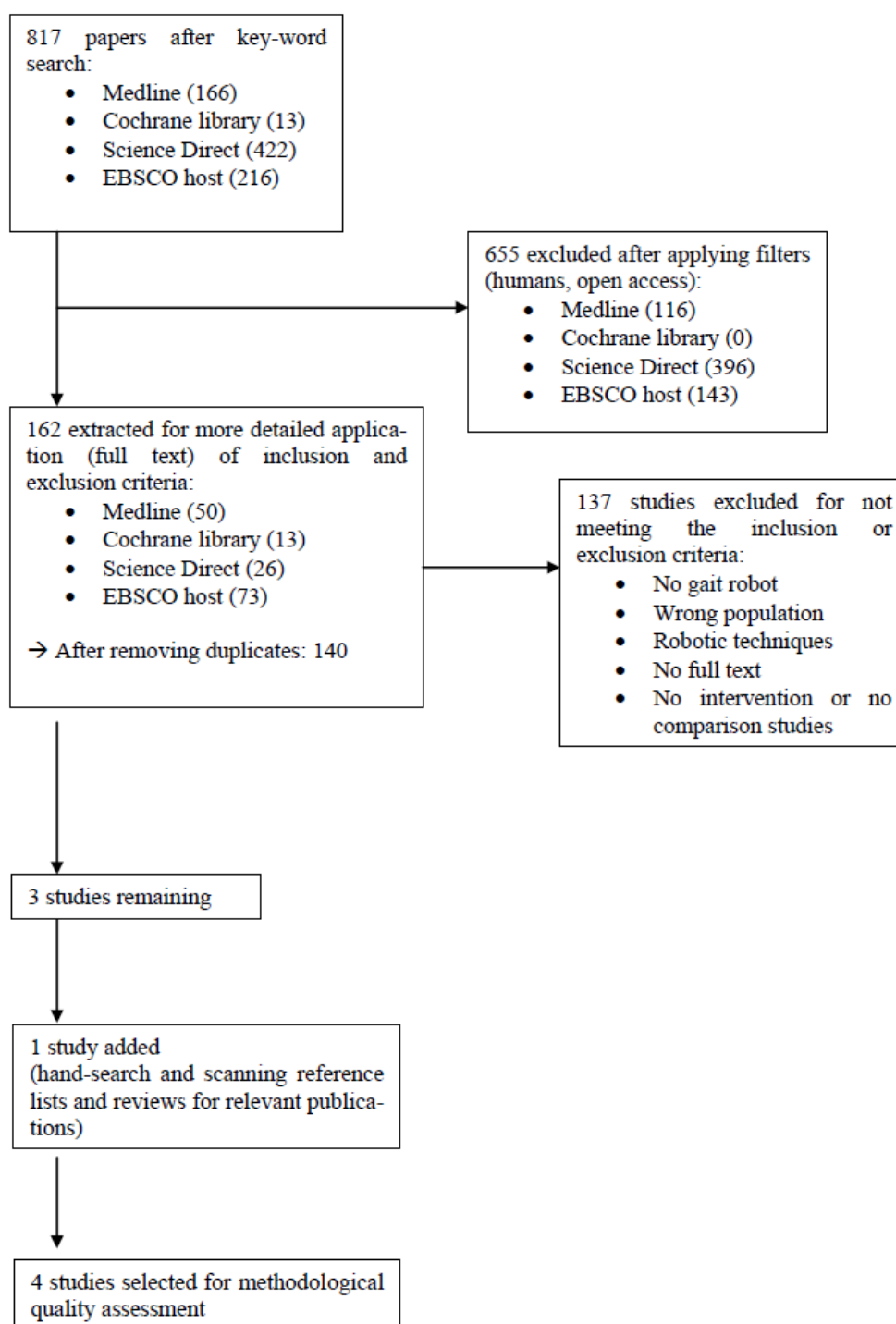


Figure 3. Flow diagram of study selection.

Only studies that included population (adults, 18+) with incomplete motor or sensory spinal cord injury, with interventions that compared exoskeleton intervention with at least one other physiotherapeutic rehabilitation method for recovery of walking were chosen. Studies included were clinical trials or randomized control trials. Exclusion criteria were complete spinal cord injuries, use of exoskeleton as an assistive device, therefore not for gait rehabilitation, and single case studies.

5.5 Methodological quality assessment

All four selected studies were assessed for quality, using the PEDro tool. PEDro is abbreviated for Physiotherapy Evidence Database, a freely available online database that contains over 37,600 studies which have been assessed using the PEDro scale. The PEDro scale contains 11 different criteria, where each is given a point when clearly applicable to the study or a zero if it is not. The first criterion is not used in the final scoring (Website of Physiotherapy Evidence Database Free Online, 1999).

Table 4. Methodological quality assessment using PEDro Scale.

| | Criteria | | | | | | | | | | | |
|-------------------------|-----------------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|-----------|--------------|
| Study | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | Score |
| Noojien et al. 2009 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 3/10 |
| Field-Fote & Roach 2011 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 6/10 |
| Labruyere & Hedel 2014 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 6/10 |
| Lam et al. 2015 | 0 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 8/10 |

After eliminating the score of the first criterion which is not used in the final scoring, two studies achieved the final score 6/10, one study achieved score 8/10 and one 3/10. Trial reports that score $\geq 6/10$ on the PEDro scale are of moderate to high quality (Website of Physiotherapy Evidence Database Free Online, 1999). Only studies which achieved at least score 6/10 were included in this review (three studies in total), therefore the study with the lowest score (trial by Noojien et al. 2009) was eliminated from the review.

Table 5: Summary of the included articles.

| Author, year of publication | Aim of the study | Study design | Subjects | Methods | Results | Limitations |
|-----------------------------|---|--|---|---|---|---|
| Field-Fote & Roach 2011 | To compare changes in walking speed and distance associated with 4 locomotor training approaches | Single-blind, randomized clinical trial. | 74 participants with chronic iSCI; injury at T10 or above, AIS C and D | Randomized to four groups: 1) treadmill-based training with manual assistance (TM; n=19), 2) treadmill-based training with stimulation (TS; n=22), 3) over-ground training with stimulation (OG; n=18), 4) treadmill-based training with robotic assistance (LR; n=15). All participants trained 5 days per week for 12 weeks (target was 60 sessions). | Walking speed: statistically significant improvement in OG, TS, and TM groups, but not in LR group. Walking distance statistically significant in OG and TS groups, but not TM and LR groups. The Lower Extremity Motor Scores (LEMS) of participants in all 4 training groups increased by 8% to 13% after the intervention. | Unknown if training dosage and emphasis on training speed were optimal (training dosage was based on clinical judgment). Configuration of robot-assisted training program imposes stepping regardless of participant's active effort. Small number of participants in post follow-up. |
| Labruyere & Hedel 2014 | To compare robot-assisted gait training (RAGT) with strength training in patients with chronic iSCI | Randomized clinical trial | Nine participants (five male, four female) with chronic iSCI, C4-T11 AIS C and D; 59 ± 11 years old | Randomized to 2 groups: group 1 (n=5): received 16 sessions of RAGT using Lokomat (45 min each) within 4 weeks followed by 16 sessions of strength | Task-specific RAGT was not better than lower extremity strength training. Maximal walking speed (assessed with 10MWT), improved | Small sample size, possible motivational bias, assessor bias. |

| | | | | | | |
|-----------------|--|--|--|--|--|-------------------|
| | | | | training (45 min each) within 4 weeks. Group 2 (n=4): received the same in reversed order. | significantly more after strength training than after RAGT. | |
| Lam et al. 2015 | To determine the feasibility and evaluate the potential efficacy of Lokomat-applied resistance (Loko-R) training on functional ambulation in people with chronic iSCI. | Double blind, Randomized control trial | 15 participants (nine male, six female) with chronic iSCI, C2-T10 AIS C and D. | Randomized to Lokomat applied resistance against the hip and knee Loko-R (test group; n=8) or Lokomat-assisted BWSTT (control group; n=7); training for both groups 45 min 3x/week for 3 months. | Loko-R group had significantly better scores in SCI-FAP (decrease by 204 points) than Control (decrease by 18 points) at posttraining and in follow-up assessment. Overground walking speed (assessed with 10MWT) increased by 0.10 m/s in both groups, and by 0.12 m/s in 1 mo and 6 mo follow-ups. Walking distance (assessed by 6MWT) increased by 19.6 m, by 42.5 m at 1 mo follow-up, and by 56.9 m at 6 mo follow-up. | Small sample size |

6 RESULTS

All three studies were intervention studies that compared robot-assisted gait training with at least one other mode of training in subjects with incomplete spinal cord injury, AIS grade C or D. All studies assessed effects of training on walking speed and walking distance as well as other outcome measures.

The study by Field-Fote & Roach (2011) compared changes in walking speed and walking distance associated with four locomotor training approaches: treadmill-based training with manual assistance (TM), treadmill-based training with stimulation (TS), overground training with stimulation (OG), and treadmill-based training with robotic assistance (LR) which used Lokomat. Each training approach provided some assistance with stepping, with Lokomat set to 100% assistance to impose a kinematically consistent gait pattern. The improvement in walking speed (assessed by 10MWT) was statistically significant for the OG, TS and TM groups but not for the LR group. The increase in walking distance (assessed by 2 minute walking test) was statistically significant for the OG and TS groups but not for the TM and LR groups. The study showed greater improvements in functional walking capacity with overground locomotor training approach than in treadmill-based training.

The study by Labruyere & Hedel (2014) compared robot-assisted gait training with conventional strength training. Group 1 received 16 sessions of robot-assisted training using Lokomat, followed by 16 sessions of strength training. Group 2 received the same but in reversed order. Strength training focused on muscles of lower extremities with exercises of isotonic leg press in supine, isotonic hip adduction, abduction, flexion and extension with or without resistance. Results showed that maximal walking speed improved more after strength training than robot-assisted training, whereas overall walking performance (walking at preferred speed) did not show any significant difference between the two approaches.

The study by Lam et al. (2015) was the only double blinded study and as such different because it compared two interventions using Lokomat: the test group used Lokomat-applied resistance (Loko-R) and the control group used conventional

Lokomat-assisted body weight-supported treadmill training. All participants improved their walking speed by 0.10 m/s post-training, by 0.12 m/s at 1 month follow-up, and by 0.09 m/s at 6 month follow-up assessments, measured with the 10MWT. Both groups improved the walking distance, where 6MWT increased by 19.6 m, by 42.5 m at 1 month follow-up, and 56.9 m at 6 month follow-up. However, there was no significant difference in these outcomes between the groups. Loko-R group showed significantly greater improvement in the Spinal Cord Injury-Functional Ambulation Profile (SCI-FAP) at post-training than the Control group: scores decreased by 204 points and in the Control group by only 18 points. Improvements were retained at 1 month and 6 months follow-up. The study showed that applied resistance to the Lokomat is a feasible method in gait rehabilitation in people with incomplete SCI and may improve skilled overground walking performance.

7 CONCLUSION

According to the studies, robot-assisted gait training using Lokomat is not more efficient in improving walking speed and walking distance compared to other physiotherapeutic modalities, such as treadmill-based training with manual assistance, treadmill-based training with stimulation, overground training with stimulation, and strength training. It appears that conventional gait training on a treadmill and muscle strength training yield better results in walking speed and distance, and overground locomotor training shows greater improvements in functional walking capacity than treadmill-based training. However, added resistance to a regular Lokomat training is a feasible method and may improve patient's overground walking performance. All studies have the same limitation, which is a small sample size.

8 DISCUSSION

Having the background of working as a personal assistant to a person with a spinal cord injury, the author found this topic to be of her special interest. In addition to that, robot-assisted therapy was observed during one of the clinical placements where a patient with incomplete spinal cord injury was engaged in gait training using the Lokomat system. From own experience with spinal cord injured patients it can be agreed that rehabilitation of gait can be very physically demanding for physiotherapists and robot-assisted rehabilitation may ease the physical input from the therapists to a great extent.

After the topic was decided, it was rather easy to find relevant publications on exoskeletons to become familiarized with the research area. The starting-point was the website Exoskeletonreport which holds extensive information on different exoskeleton models and points to further literature search on robotics in medicine which was used in the theoretical part.

The search process in the literature review was demanding because it was lacking studies which would compare exoskeletons with other physiotherapeutic approaches. After many unsuccessful attempts to find more publications, the key-words were set to have a wider meaning which in return yielded numerous results. Those were scanned through manually by reading titles or abstracts. In the end, there were only three studies included in the review but this is in concordance with other literature reviews on exoskeletons which also claim that there have not been enough clinical trials done yet. However, only freely available articles were included in the review and there might have been more studies found without applying this filter.

As exoskeletons are a fairly recent mode in physiotherapy, it was decided not to limit the criteria with year of publications and instead approve all applicable studies regardless of year of publication. However, all three studies were published recently, that is in 2011, 2014 and 2015. Unfortunately, all three studies investigated the same exoskeleton (Lokomat) which was in contrast with the initial intention of this thesis. It was being expected to find more studies with mobile exoskeletons instead of a

fixed, treadmill based such as Lokomat. That was also the reason why more theory was devoted to fixed exoskeletons than it was intended. The initial plan was to make a literature review on mobile exoskeletons rather than fixed ones.

The biggest limitation of this review is the small number of studies. There are only three studies included in the review, and one of them compared standard Lokomat with Lokomat-applied resistance. The latter is not an independent physiotherapeutic modality per se but the added resistance to the Lokomat does imply another modality which is resistance training and it was therefore included in the review. Small study number leads to another limitation, which is that the robot-assisted therapy is compared to many different interventions within one study. It would be easier to draw conclusions on effectiveness of robot-assisted therapy if it was compared to the same intervention in all three studies.

What needs to be done in future, are more good quality studies with larger number of participants that compare an exoskeleton with another therapeutic modality. There should also be more studies conducted which would compare a mobile exoskeleton, instead of a fixed one, with other therapeutic modality. Most studies so far are based on research whether a certain exoskeleton is a safe and feasible option in gait rehabilitation.

Furthermore, if SAMK does purchase an exoskeleton, another possible thesis topic could be evaluating that particular exoskeleton for other populations than spinal cord injury, e.g. multiple sclerosis, stroke, cerebral palsy and other neurological conditions that affect walking. Apart from physiotherapy students, the exoskeleton can be interesting also for engineering students and staff.

All in all, this thesis can provide a deeper insight in the possibility to combine technology with conventional physiotherapy in locomotor rehabilitation. With further development of exoskeletons to be more user-friendly, have lower price and achieve better speed they may someday replace wheelchairs as a new assistive device.

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